Consideration Of Previously Submitted Information Disclosure Statement

It is noted that an initialed copy of the PTO Form 1449 that was submitted with Applicant's Information Disclosure Statement filed October 4, 1999 has not been returned to Applicant's representative with the Office Action. Accordingly, it is requested that an initialed copy of the Form 1449 be forwarded to the undersigned with the next communication from the PTO. In order to facilitate review of the references by the Examiner, a copy of the Information Disclosure Statement and the Form 1449 are attached hereto. Copies of the cited references were provided at the time of filling the original Information Disclosure Statement, and, therefore, no additional copies of the references are submitted herewith. Applicants will be pleased to provide additional copies of the references upon the Examiner's request if it proves difficult to locate the original references.

Claim Disposition

Claims 1-4, 6, 9, 16, and 17 are amended.

New Claim 24 is added.

Claims 1-24 are now pending in the application.

No new matter has been added by way of amendment. Reconsideration and reexamination of the application, in light these amendments as more fully explained below, is requested.

The Invention

The presently claimed invention is related to compositions for expression of genes in plants. The compositions of the invention are related to promoter sequences that drive expression in plants. The promoter sequences natively drive expression of a plant cell death suppressor gene in a plant cell. More particularly, the compositions of the claimed invention include the sequence set forth in SEQ ID NO:1. Expression cassettes, vectors, and host cells comprising these sequences are encompassed by the invention. Transformed plants and seeds thereof comprising these sequences are also encompassed by the invention.

The Rejections of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

Written Description

Claims 1-23 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in a manner reasonably conveying to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. As a basis for this rejection, the Office Action indicates that the described 5′ region of the *lls1* gene, fails to provide an adequate written description for the claims, as broadly drawn. The Office Action further indicates that the specification does not describe the structure of promoters from other plant cell death suppressor genes, and cites *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed Cir. 1997) in support.

This rejection is traversed. Nevertheless, for the purpose of facilitating prosecution, the claims have been amended as set forth above, and the rejection obviated by amendment. Independent claim 1 is amended to include a limitation drawn to a promoter sequence comprising the sequence set forth in SEQ ID NO:1, in addition to including limitations drawn to a promoter sequence that drives expression of a gene in a plant cell wherein the promoter sequence natively drives the expression of a plant cell death suppressor protein. Claim 2 is amended to independent form, and is drawn to an isolated nucleotide sequence comprising the sequence set forth in SEQ ID NO:1. Support for these amendments can be found throughout the specification, including the sequence listing, and the original claims. Independent claims 9 and 17, as originally filed, also contain limitations drawn to SEQ ID NO:1. Accordingly, all present claims include a limitation drawn to the sequence set forth in SEQ ID NO: 1. Applicants were clearly in possession of this sequence at the time the application was filed.

The office action further indicates that applicants have not shown promoter activity for the claimed 5′ upstream region of the *lls1* gene. Applicants respectfully submit that the determination of adequate written description is not based on the presence or absence of a working example, and the law is well settled that that the enablement and written description requirements of 35 U.S.C. §112, first paragraph are separate and distinct.

As indicated above, the specification clearly sets forth the sequence for the presently claimed invention (SEQ ID NO:1). As acknowledged on page 3 of the Office Action, the specification also describes that SEQ ID NO:1 corresponds is the 5′ upstream region of the *lls1* gene. The specification also describes that the sequence set forth in SEQ ID NO:1 is a promoter, and that the promoter is useful for driving any gene in a plant cell. See, for example, lines 19-28, page 15, of the specification. Page 24, lines 22-28, describes a 7,129 bp genomic clone identified by Genbank Account No. U77346, and likely to contain the *lls*1 promoter. Page 25, lines 2-4, of the specification indicates that the transcription start site occurs at position 3115 of the 7,129 clone. A person of ordinary skill in the art would interpret these descriptions in the specification to mean that the promoter region responsible for activating and driving expression of the *lls1* gene would include and extend upstream of bp 3114.

An examination of the sequences set forth in SEQ ID NO:1 and Genbank Account number U77346 reveals that SEQ ID NO:1 corresponds to the contiguous 2,822 bp region upstream of the transcription initiation site for the *lls1* gene. Accordingly, the specification describes a 2,822 genomic sequence that is directly upstream of the transcription initiation site.

Applicants submit that it is well known, and was well known at the time the application was filed, that regions responsible for activating and driving expression would be well within a 2,822 bp region upstream of a transcription initiation region. Typically, canonical TATA and CAAT boxes are found within about 100 base pairs of the transcription initiation region, in eucaryotes. Furthermore, as acknowledged on page 4, lines 15-17, of the Office Action, the specification teaches that the *lls1* gene is expressed, and induced by wounding and *H. carbonum* infection. Therefore, Applicants respectfully submit that considering the length of the contiguous genomic sequence set forth in SEQ ID NO:1, and its position being directly upstream of the transcription initiating site of an actively expressed cell death suppressor gene *in vivo* in a plant, provides adequate written description for a sequence that drives expression of a gene in a plant cell.

Furthermore, new claim 24 is added, which claim is drawn to include limitations drawn to a promoter sequence that drives expression of a gene in a plant cell, and hybridizes to the

complement of the sequence set forth in SEQ ID NO:1. Thus, the claim includes limitations drawn to structural as well as functional features. Support for the new claims can be found throughout the specification as originally filed. For example, see line 3, page 6 to line 4, page 7 of the specification.

Therefore, in light of the above amendments and remarks, Applicants submit that the specification reasonably conveys to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, Applicants request that this rejection of the present claims under consideration be withdrawn, and not extended to the newly submitted claims.

Enablement

Claims 1-23 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. As a basis for this rejection, the Office Action indicates that Applicant does not teach that SEQ ID NO:1 has promoter activity and can activate expression of an operably linked coding sequence. The Office Action further indicates that the specification does not teach promoters from other plant cell death suppressor genes, as broadly claimed. The Office Action cites Benfey *et al.* (1990) *Science 250*: 959-966, Abstract, Fig.3-5; and kim *et al.* (1994) *Plant Mol. Biol. 24*: 105-117, Abstract, Tables 1-4, Fig.1-2; in support of region specificity of promoter activity, and empirical nature of promoter isolation.

First, Applicants note that an enabling disclosure needs to describe the claimed invention in such a way as to enable the ordinarily skilled artisan to make and use the invention commensurate with the scope of the claims. There is no requirement that the disclosure describe how the invention works. Nor is a working example of every permutation of the invention a requirement.

As more fully explained above, under *Written Description*, all independent claims include a limitation drawn to SEQ ID NO:1. Independent claim 1 is amended to include a limitation drawn to a promoter sequence comprising the sequence set forth in SEQ ID NO:1, in addition to including limitations drawn to a promoter sequence that drives expression of a gene

in a plant cell wherein the promoter sequence natively drives the expression of a plant cell death suppressor protein. Claim 2 is amended to independent form, and is drawn to an isolated nucleotide sequence comprising the sequence set forth in SEQ ID NO:1. Independent claims 9 and 17 also contain limitations drawn to SEQ ID NO:1 and are directed to plants and plant cells comprising the sequence of the invention. In light of the disclosure of SEQ ID NO:1, the specification fully enables one of ordinary skill in the art how to make this composition.

In contrast to the statements in the Office Action, the specification explicitly teaches that SEQ ID NO:1 is a promoter, and can drive the expression of operably linked coding sequences. See page 15 of the specification. Furthermore, page 7, line27, to page 8, line 31 describes construction of expression cassettes for plant transformation; and page 9 to page 10, line 10, describes plant transformation methods. Thus, taken as a whole, the specification provides an enabling disclosure of how to use the sequences of the invention to drive expression in a plant cell.

As more fully explained above, SEQ ID NO:1 is a 2,822 bp contiguous genomic sequence directly upstream of the transcription initiating site of an actively expressed cell death suppressor gene *in vivo* in a plant. The length, contiguity, and the description of the *in vivo* activity of the gene support promoter activity for SEQ ID NO:1. Further in support, Applicants submit for consideration well known examples of 5′ flanking regions of plant genes that are about 1.2 kbp or less, and were selected for promoter analysis by those skilled in the art. See for example, pages 106, 291, and 503, in *Control of Plant Gene Expression* (1993), ed. Desh Pal Verma, CRC Press; copies attached herewith.

Applicants further note that regulatory elements described in Benfey *et al.* and Kim *et al.* cited in the present Office Action are positioned within about one- to several hundred bases upstream of the transcription initiation site. Thus, the Office Action has not provided any evidence of plant regulatory sequences that are essential for activating and driving expression, that are located several thousand bp from the transcription start site.

Furthermore, lines 2-5 on page 16 of the specification provide that promoter activity can be determined by assaying for expression of a an operably linked reporter gene. Applicants

submit that, as is evident from Benfey *et al.* and Kim *et al.*cited in the present Office Action, such methods of assaying for plant promoter activity was well known in the art An ordinarily skilled artisan can test for promoter activity of SEQ ID NO:1 by routine methods, and without undue experimentation.

Therefore, in light of the above amendments and remarks, Applicants submit that the specification enables an ordinarily skilled artisan how to make and use the claimed invention commensurate with the scope of the claims. Accordingly, Applicants respectfully request that this rejection of the claims be withdrawn, and not extended to the newly submitted claims.

The Rejections of the Claims Under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 1-8 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Claim 1 was rejected for recitation of the phrase "is capable of driving". This rejection of is obviated by amending the claim to change the phrase to --drives--, as suggested by the examiner.

Claim 2 was rejected for recitation of the phrase "The promoter of claim 1" without proper antecedent basis. This rejection of is obviated by amending the claim to independent form as set forth above.

Claim 3 was rejected for recitation of the phrase "The promoter of claim 1" without proper antecedent basis. This rejection of is obviated by amending the claim to read --the nucleotide sequence of claim 2--.

Claim 4 is rejected for recitation of the phrase "DNA construct". This rejection is obviated by replacing the phrase with --expression cassette--. Claim 3 has likewise been amended to provide proper antecedent basis. Claims 6, 9, and 17 have been likewise amended for consistency. Support for these amendments can be found, for example, on page 7, line27, to page 8, line 31 in combination with page 15 of the specification.

Claim 6 is rejected for recitation of the phrase "DNA construct" without proper antecedent basis. This rejection is obviated as explained in the preceding paragraph..

Applicants further note that claim 16 is amended to replace the word "Seed" with--

Transformed seed--. The amendment is supported, for example, by original claim 8.

CONCLUSIONS

Accordingly, in view of the above remarks and amendments, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. § 112, first and second paragraphs are overcome. Applicants respectfully submit that this Application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to cal the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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CONTROL *of* PLANT GENE EXPRESSION

Edited by

Desh Pal S. Verma

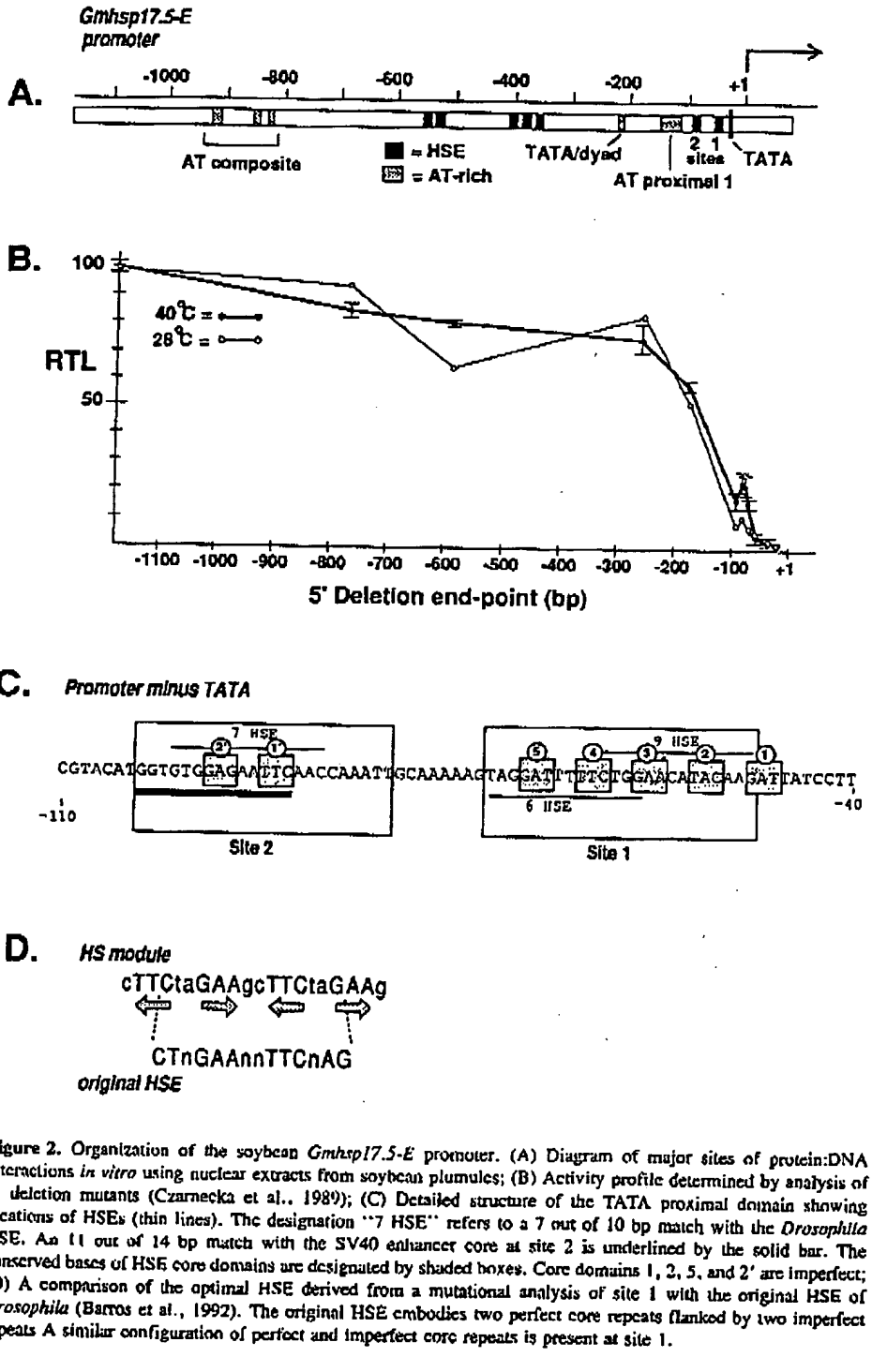

Figure 2. Organization of the soybean *Gmhsp17.5-E* promoter. (A) Diagram of major sites of protein:DNA interactions *in vitro* using nuclear extracts from soybean plumules; (B) Activity profile determined by analysis of 5' deletion mutants (Czarnecka et al., 1989); (C) Detailed structure of the TATA proximal domain showing locations of HSEs (thin lines). The designation "7 HSE" refers to a 7 out of 10 bp match with the *Drosophila* HSE. An 11 out of 14 bp match with the SV40 enhancer core at site 2 is underlined by the solid bar. The conserved bases of HSE core domains are designated by shaded boxes. Core domains 1, 2, 5, and 2' are imperfect; (D) A comparison of the optimal HSE derived from a mutational analysis of site 1 with the original HSE of *Drosophila* (Barros et al., 1992). The original HSE embodies two perfect core repeats flanked by two imperfect repeats A similar configuration of perfect and imperfect core repeats is present at site 1.

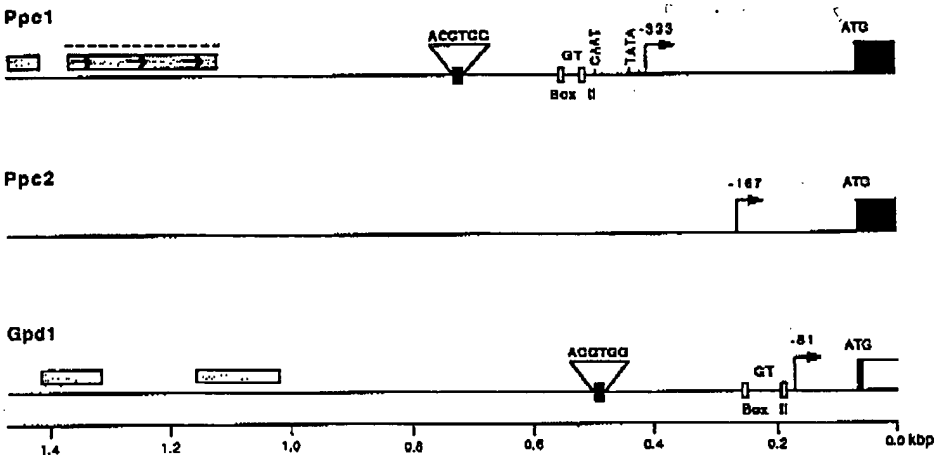

Figure 2. Schematic diagram of the 5' upstream regions of three genes from *M. crystallinum*. The transcriptional start site (+1) of each gene is designated with a large arrow. Exons and introns in the 5' coding regions are denoted by closed or open boxes, respectively. ABRE's motifs are designated by the conserved sequence motif above black boxes. GT motifs (boxes II) are designated by open boxes. Conserved regions of intermittent sequence homology common to both the *Ppc*1 and *Gpd*1 genes are designated by shaded boxes. Direct repeat sequences are designated with small arrows.

STRUCTURE OF THE 5' FLANKING REGIONS OF THREE GENES FROM THE COMMON ICE PLANT

As a first step in the analysis of the mechanism of CAM gene induction, we have determined the sequences of the 5' flanking regions of the *Ppc*1, *Ppc*2, and *Gpd*1 genes (Figure 2). The transcriptional start sites of these genes were determined by primer extension analysis (Dean et al., 1987). The transcriptional start site of *Ppc*1 is 333 nt upstream of the translational start codon. This 5' untranslated leader sequence is unusually long and may be important to the stability of the transcript and thus play a posttranscriptional role in influencing expression. The *Ppc*2 untranslated leader is 167 nt in length and that of the *Gpd*1 gene is 81 nt in length. The *Ppc*1 5' flanking region contains obvious consensus TATA (i.e., TATAAAA) and CAAT box (i.e., CCAAT) motifs at −33 and −106, respectively (Joshi, 1987). TATA and CAAT consensus motifs are not obvious in the *Ppc*2 and *Gpc*1 genes. The absence of good consensus motifs in housekeeping genes encoding enzymes has been observed in animal systems. The *Ppc*2 gene encodes a housekeeping enzyme (Cushman and Bohnert, 1989) and the single *Gpd*1 gene product apparently functions in both a housekeeping and an inducible CAM capacity (Ostrem et al., 1990).

The 5' flanking and leader regions of the *Ppc*1, *Ppc*2, and *Gpd*1 genes display several interesting features (Figure 2). One type of *cis*-element motif shows similarity to the GT motif (Box II), a conserved motif having the consensus GTGTGGTTAAT which functions in light-responsive gene expression (Lam and Chua, 1990). Related sequences are present twice in the upstream regions of both *Ppc*1 and *Gpd*1, but are conspicuously absent from the *Ppc*2 promoter region. Large regions of intermittent sequence similarity are found in regions far upstream of the *Ppc*1 and *Gpd*1 transcript start sites. These regions of similarity lie in the area of a triple tandem direct repeat sequence of 14 bp (Figure 2) found in the *Ppc*1 gene. This region has been shown, by *in vivo* transient expression assays using microprojectile bombardment of intact leaves, to contain enhancer activity for the *Ppc*1

TABLE 1.
Amino Acid Compositions (Expressed as mol%) of the Groups of Hordein Polypeptides

	B	C	D	γ "r"	γ "m + q"
Asp[a]	1.4	1.0	1.3	2.9	2.8
Thr	2.1	1.0	8.1	3.1	2.1
Ser	4.7	4.6	9.7	5.5	5.7
Glu[b]	35.4	41.2	29.6	32.4	29.9
Pro	20.6	30.6	11.6	16.5	22.1
Gly	1.5	0.3	15.7	5.9	2.5
Ala	2.2	0.7	2.5	2.6	2.2
Cys	2.5	0	1.5	2.7	3.3
Val	5.6	1.0	4.5	3.7	5.5
Met	0.6	0.2	0.2	1.2	1.2
Ile	4.1	2.6	0.7	2.9	2.5
Leu	7.0	3.6	3.3	8.6	6.9
Tyr	2.5	2.3	3.9	1.7	2.1
Phe	4.8	8.8	1.4	4.7	6.1
His	2.1	1.1	3.4	2.0	1.6
Lys	0.5	0.2	1.1	1.6	1.2
Arg	2.4	0.8	1.5	2.0	2.5
% Amidation of asp + glu	90	92	nd	nd	nd
References	1	2	3	4	4

[a] Includes Asn
[b] Includes Gln
(1) Total B hordein from cv. Julia (Shewry et al., 1980); (2) Total C hordein from cv. Julia (Shewry et al., 1980); (3) D Hordein from Risø mutant 1508 (Kreis et al., 1984); (4) γ-Hordein bands from Risø 56 (Kreis et al., 1983).
nd = not determined; tryptophan was not determined.

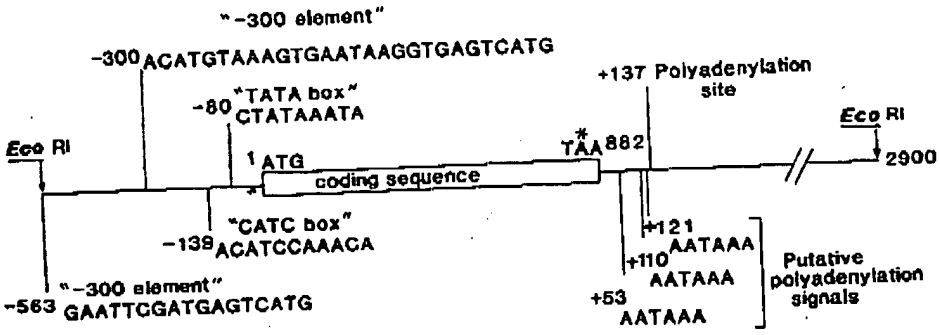

Figure 2. The structure of a B hordein gene from cv. Sundance (based on data in Forde et al., 1985).

tobacco using *Agrobacterium tumefaciens*. B1 hordein transcripts were detected in the seeds but not the leaves, hordein protein, however, was not detected (Shewry et al., 1988b). They also fused 549 bp of the immediate 5′ upstream region to the CAT reporter gene and showed that CAT activity was only detected in the endosperm of the developing seed (not in the embryo, testa, or vegetative tissues), about 15 days after pollination (Marris et al.,